

Page 6, third paragraph:

In a series of studies, Tansy was able to demonstrate that polyamines have a profound impact on the motility of the gastrointestinal (GI) tract. The original work focused on poly(ethylenimine) and gastric emptying in rodents and dogs. Branched-chain poly(ethylenimine)s effected significant inhibition of gastric emptying in rodents; however, they caused a severe retch response in dogs. Because of the structural relationship between the poly(ethylenimine)s and natural polyamines, Tansy elected to evaluate the effect of spermidine, spermine, and a group of polyamine analogues on the gastric emptying of rodents. It soon became clear that polyamines had a substantial influence on gastric emptying and that "endogenous spermine and spermidine may have some unrecognized GI secretomotor activity". [See Spermine and Spermidine as Inhibitors of Gastrointestinal Motor Activity, Surg. Gyn. Obst, **1982**, 154, 74-80; Pharmacology of Polyethylenimine I: Effects on Gastric Emptying In Rats, J. Pharm. Sci. **1977**, 66, 899-901; GI Pharmacology of Polyethylenimine II: Motor Activity in Anesthetized Dogs, J. Pharm Sci. **1977**, 66, 902-904; Effects of Spermine and Spermidine on Gastric Emptying in Rats, J. Pharm. Sci **1981**, 70 347]. From a structure-activity perspective, it also became obvious that minor changes in the polyamine's structure could completely eradicate the molecule's ability to inhibit gastric emptying. These studies strongly suggested that the polyamine pharmacophore was an excellent candidate for the construction of antitransit, antidiarrheal drugs.